# IUCLID

# Data Set

| | | |
|---|---|---|
| **Existing Chemical** | : | ID: 108-20-3 |
| **CAS No.** | : | 108-20-3 |
| **EINECS Name** | : | diisopropyl ether |
| **EC No.** | : | 203-560-6 |
| **TSCA Name** | : | Propane, 2,2'-oxybis- |
| **Molecular Formula** | : | C6H14O |

**Producer related part**

| | | |
|---|---|---|
| **Company** | : | ExxonMobil Biomedical Sciences Inc. |
| **Creation date** | : | 18.05.2005 |

**Substance related part**

| | | |
|---|---|---|
| **Company** | : | ExxonMobil Biomedical Sciences Inc. |
| **Creation date** | : | 18.05.2005 |
| **Status** | : | |
| **Memo** | : | HPV |
| **Printing date** | : | 12.12.2005 |
| **Revision date** | : | |
| **Date of last update** | : | 12.12.2005 |
| **Number of pages** | : | 47 |
| **Chapter (profile)** | : | Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10 |
| **Reliability (profile)** | : | Reliability: without reliability, 1, 2, 3, 4 |
| **Flags (profile)** | : | Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS |

### 1.0.1 APPLICANT AND COMPANY INFORMATION

### 1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

### 1.0.3 IDENTITY OF RECIPIENTS

### 1.0.4 DETAILS ON CATEGORY/TEMPLATE

### 1.1.0 SUBSTANCE IDENTIFICATION

### 1.1.1 GENERAL SUBSTANCE INFORMATION

| | | |
|---|---|---|
| **Purity type** | : | |
| **Substance type** | : | organic |
| **Physical status** | : | liquid |
| **Purity** | : | |
| **Colour** | : | |
| **Odour** | : | |

27.10.2005

### 1.1.2 SPECTRA

### 1.2 SYNONYMS AND TRADENAMES

**2,2'-oxybis-propane**

27.10.2005

**2,2'-oxybispropane**

27.10.2005

**2-Isopropoxy Propane**

27.10.2005

**2-Isopropoxypropan**

27.10.2005

**2-isopropoxypropane**

27.10.2005

**Diisopropyl Ether**

27.10.2005

**Dipropyloxid**

27.10.2005

**IPE**

27.10.2005

**IPE; Diisopropylether; DIPE; 2-Isopropoxy propane**

27.10.2005

**Isopropyl Ether**

27.10.2005

**Isopropylether**

27.10.2005

**propane, 2,2'-oxybis-**

27.10.2005

**1.3 IMPURITIES**

**1.4 ADDITIVES**

**1.5 TOTAL QUANTITY**

**1.6.1 LABELLING**

**1.6.2 CLASSIFICATION**

**1.6.3 PACKAGING**

**1.7 USE PATTERN**

**1.7.1 DETAILED USE PATTERN**

**1.7.2 METHODS OF MANUFACTURE**

**1.8 REGULATORY MEASURES**

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

## 2.1 MELTING POINT

| | | |
|---|---|---|
| **Value** | : | = -86.8 °C |
| **Sublimation** | : | |
| **Method** | : | other: not specified |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS # 108-20-3) |
| **Test substance** | : | CAS No. 108-20-3; diisopropyl ether; purity is unknown. |
| **Reliability** | : | (2) valid with restrictions<br>The CRC Handbook of Chemistry and Physics is a peer reviewed publication. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure. |
| **Flag** | : | Critical study for SIDS endpoint |

07.12.2005 (19)

## 2.2 BOILING POINT

| | | |
|---|---|---|
| **Value** | : | = 68.5 °C at 1013 hPa |
| **Decomposition** | : | |
| **Method** | : | other: not specified |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS: Diisopropylether |
| **Test substance** | : | CAS No. 108-20-3; diisopropyl ether; purity is unknown. |
| **Reliability** | : | (2) valid with restrictions<br>The CRC Handbook of Chemistry and Physics is a peer reviewed publication. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure. |
| **Flag** | : | Critical study for SIDS endpoint |

27.10.2005 (19)

## 2.3 DENSITY

| | | |
|---|---|---|
| **Type** | : | density |
| **Value** | : | = .7241 g/cm³ at 20 °C |
| **Method** | : | other: not specified |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS # 108-20-3) |
| **Test substance** | : | CAS No. 108-20-3; diisopropyl ether; purity is unknown. |
| **Reliability** | : | (2) valid with restrictions<br>The CRC Handbook of Chemistry and Physics is a peer reviewed publication. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure. |
| **Flag** | : | Critical study for SIDS endpoint |

07.12.2005 (19)

### 2.3.1 GRANULOMETRY

## 2.4 VAPOUR PRESSURE

| | | |
|---|---|---|
| **Value** | : | = 198.65 hPa at 25 °C |
| **Decomposition** | : | |
| **Method** | : | |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS # 108-20-3) |
| **Method** | : | Method not specified. |
| **Test substance** | : | CAS No. 108-20-3; diisopropyl ether; purity is unknown. |
| **Reliability** | : | (2) valid with restrictions<br>This robust summary has a reliability rating of 2 because the data were not reviewed for quality, however, the reference is from a peer-reviewed handbook. |
| **Flag** | : | Critical study for SIDS endpoint |

07.12.2005 (6)

## 2.5 PARTITION COEFFICIENT

| | | |
|---|---|---|
| **Partition coefficient** | : | octanol-water |
| **Log pow** | : | = 1.52 at 25 °C |
| **pH value** | : | |
| **Method** | : | other (measured) |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS: Diisopropylether |
| **Method** | : | Method not specified. |
| **Test substance** | : | CAS No. 108-20-3; diisopropyl ether; purity is unknown. |
| **Reliability** | : | (2) valid with restrictions<br>The value cited by the authors is a measured and preferred value. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure. |
| **Flag** | : | Critical study for SIDS endpoint |

27.10.2005 (15)

| | | |
|---|---|---|
| **Partition coefficient** | : | octanol-water |
| **Log pow** | : | = 2.4 at °C |
| **pH value** | : | 6.7 |
| **Method** | : | other (calculated): Indirect method by reverse-phase HPLC |
| **Year** | : | |
| **GLP** | : | no |
| **Test substance** | : | other TS: diisopropyl ether (CAS No. 108-20-3) |
| **Result** | : | Log Pow = 2.4 (Pow = 250) at pH 6.7 |
| **Test condition** | : | The HPLC system was a reverse-phase C18-coated silica gel column, 250 mm x 5 mm id, with a mobile phase of 3 volumes methanol and 1 volume water (final pH 6.7) at a flow rate of 1 mL/min. 100 mL samples of an approximate 1 mg/mL solution in the mobile phase were injected, and the emergence of the material was observed using refraction index detection. Thirty-one reference compounds were used to generate the linear relationship between log k (k = capacity factor) and log Pow. Using the HPLC retention time for the peak of the test substance, the log k was determined, and the log Pow value was calculated using the linear equation developed from the reference compounds.<br><br>Log Pow was determined according to the following calculations:<br>Retention time (RT), min = 5.7 |

Capacity factor, k = 0.87, k = (RTcmpd - RTunretained std)/RTunretained std
log k = -0.06
linear equation: log k = -0.930 + 0.357 log Pow

**Reliability** : (1) valid without restriction
12.12.2005 (8)

### 2.6.1 SOLUBILITY IN DIFFERENT MEDIA

| | | |
|---|---|---|
| **Solubility in** | : | Water |
| **Value** | : | = 8800 mg/l at 20 °C |
| **pH value** | : | |
| **concentration** | : | at °C |
| **Temperature effects** | : | |
| **Examine different pol.** | : | |
| **pKa** | : | at 25 °C |
| **Description** | : | |
| **Stable** | : | |
| **Deg. product** | : | |
| **Method** | : | |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS # 108-20-3) |

**Test substance** : CAS No. 108-20-3; diisopropyl ether; purity is unknown.
**Reliability** : (2) valid with restrictions
The Ullmann's Encyclopedia of Industrial Chemistry is a peer reviewed publication. This robust summary has a reliability rating of 2 because there is insufficient information available on the method and analytical procedure.
**Flag** : Critical study for SIDS endpoint
07.12.2005 (13)

### 2.6.2 SURFACE TENSION

### 2.7 FLASH POINT

### 2.8 AUTO FLAMMABILITY

### 2.9 FLAMMABILITY

### 2.10 EXPLOSIVE PROPERTIES

### 2.11 OXIDIZING PROPERTIES

### 2.12 DISSOCIATION CONSTANT

### 2.13 VISCOSITY

## 2.14 ADDITIONAL REMARKS

### 3.1.1 PHOTODEGRADATION

| | | |
|---|---|---|
| **Type** | : | air |
| **Light source** | : | |
| **Light spectrum** | : | nm |
| **Relative intensity** | : | based on intensity of sunlight |
| **Conc. of substance** | : | at 25 °C |
| **INDIRECT PHOTOLYSIS** | | |
| **Sensitizer** | : | OH |
| **Conc. of sensitizer** | : | 1500000 molecule/cm³ |
| **Rate constant** | : | = .00000000002434 cm³/(molecule*sec) |
| **Degradation** | : | = 50 % after 5.3 hour(s) |
| **Deg. product** | : | |
| **Method** | : | other (calculated): Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.12 |
| **Year** | : | |
| **GLP** | : | |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS # 108-20-3) |
| **Method** | : | Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.12<br><br>Indirect photodegradation, or atmospheric oxidation potential, is based on the structure-activity relationship methods developed by R. Atkinson under the following conditions:<br>Temperature: 25°C<br>Sensitizer: OH- radical<br>Concentration of Sensitizer: 1.5E6 OH- radicals/cm3 |
| **Remark** | : | DIPE has the potential to volatilize to air, based on a vapor pressure of 19,865 Pa at 25°C (Daubert and Danner, 1989), where it is subject to atmospheric oxidation. In air, DIPE can react with photosensitized oxygen in the form of hydroxyl radicals (OH-). The computer program AOPWIN (atmospheric oxidation program for Microsoft Windows) (EPIWIN, 2000) calculates a chemical half-life for a 12-hour day (the 12-hour day half-life value normalizes degradation to a standard day light period during which hydroxyl radicals needed for degradation are generated), based on an OH- reaction rate constant and a defined OH- concentration.<br>DIPE has a calculated half-life in air of 5.3 hours or 0.4 days (12-hour day), based on a rate constant of 24.34 E-12 cm3/molecule*sec and an OH- concentration of 1.5 E5 OH-/cm3. |
| **Reliability** | : | (2) valid with restrictions<br>The value was calculated based on chemical structure as modeled by EPIWIN. This robust summary has a reliability rating of 2 because the data are calculated and not measured. |
| **Flag** | : | Critical study for SIDS endpoint |
| 07.12.2005 | | (11) |
| **Deg. product** | : | |
| **Method** | : | |
| **Year** | : | |
| **GLP** | : | |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS # 108-20-3) |
| **Method** | : | Technical discussion |
| **Remark** | : | Direct photochemical degradation occurs through the absorbance of solar radiation by a chemical substance in aqueous solution. If the absorbed energy is high enough, then the resultant excited state of the chemical may undergo a transformation. A prerequisite for direct photodegradation is the ability of one or more bonds within a chemical to absorb ultraviolet |

(UV)/visible light in the 290 to 750 nm range. Light wavelengths longer than 750 nm do not contain sufficient energy to break chemical bonds, and wavelengths below 290 nm are shielded from the earth by the stratospheric ozone layer (Harris, 1982a).
An approach to assessing the potential for a substance to undergo photochemical degradation is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by constituent molecules (Zepp and Cline, 1977). The oxygen non-bonding electrons in ethers do not give rise to absorption above 160 nm, which is why pure ether solvents can be used in spectroscopic studies.
Consequently, DIPE is not subject to photolytic processes in the aqueous environment.

**Reliability** : (2) valid with restrictions
This robust summary has a reliability of 2 because it is a technical discussion and not a study.

**Flag** : Critical study for SIDS endpoint
07.12.2005 (33)

### 3.1.2 STABILITY IN WATER

**Type** : abiotic
**t1/2 pH4** : at °C
**t1/2 pH7** : at °C
**t1/2 pH9** : at °C
**Deg. product** :
**Method** : other: Technical discussion
**Year** :
**GLP** : no data
**Test substance** : other TS: Diisopropyl Ether (CAS # 108-20-3)

**Result** : Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals with leaving groups that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Gould, 1959). The lack of a suitable leaving group renders a compound resistant to hydrolysis. DIPE is resistant to hydrolysis because it lacks a functional group that is hydrolytically reactive and Harris (1982b) identifies ether groups as generally resistant to hydrolysis. Therefore, hydrolysis will not contribute to the removal of diisopropyl ether from the environment.

**Reliability** : (2) valid with restrictions
This robust summary has a reliability of 2 because it is a technical discussion and not a study.

**Flag** : Critical study for SIDS endpoint
07.12.2005 (14) (16)

### 3.1.3 STABILITY IN SOIL

### 3.2.1 MONITORING DATA

### 3.2.2 FIELD STUDIES

### 3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

**Type** :
**Media** : other: air - biota - sediment(s) - soil - water
**Air** : % (Fugacity Model Level I)
**Water** : % (Fugacity Model Level I)
**Soil** : % (Fugacity Model Level I)
**Biota** : % (Fugacity Model Level II/III)
**Soil** : % (Fugacity Model Level II/III)
**Method** : other: Calculation according Mackay, Level I
**Year** :

**Remark** : Physicochemical data used in the calculation:

Parameter Value w/ Units

Molecular Weight = 102.18
Temperature = 25° C
Log Kow = 1.52
Water Solubility = 8,800 g/m3
Vapor Pressure = 19,865 Pa
Melting Point = -86.8° C

**Result** : Using the Mackay Level I calculation, the following distribution is predicted for diisopropyl ether:

| %Distribution | Compartment |
|---|---|
| 97.83 | Air |
| 2.10 | Water |
| 0.06 | Soil |
| <0.01 | Sediment |
| <0.01 | Suspended Sediment |
| <0.01 | Biota |

**Test substance** : Diisopropyl Ether (CAS # 108-20-3)
**Reliability** : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.
**Flag** : Critical study for SIDS endpoint
07.12.2005 (22)

**Type** : fugacity model level III
**Media** : other
**Air** : % (Fugacity Model Level I)
**Water** : % (Fugacity Model Level I)
**Soil** : % (Fugacity Model Level I)
**Biota** : % (Fugacity Model Level II/III)
**Soil** : % (Fugacity Model Level II/III)
**Method** : other: Level III simulation using the Mackay Multimedia Environmental Model (Mackay, 2001)
**Year** :

**Method** : Level III simulation using the Mackay Multimedia Environmental Model (Mackay, 2001). Mass balances are calculated for the four bulk media of air (gas + aerosol), water (solution + suspended sediment + biota), soil, (solids + air + water), and sediment (solids + pore water). Equilibrium exists within, but not between media. Physical-chemical properties are used to quantify a chemical's behavior in an evaluative environment. Three types of chemicals are treated in this model: chemicals that partition into all media (Type 1), non volatile chemicals (Type 2), and chemicals with zero, or near-zero, solubility (Type 3). The model can not treat ionizing or speciating substances. The Level III model assumes a simple, evaluative environment with user-defined volumes and densities for the following homogeneous environmental media (or compartments): air, water, soil, sediment, suspended sediment, fish and aerosols.

This model provides a description of a chemical's fate including the important degradation and advection losses and the intermedia transport processes. The distribution of the chemical between media depends on how the chemical enters the system, e.g. to air, to water, or to both. This mode of entry also affects persistence or residence time.

The rates of intermedia transport are controlled by a series of 12 transport velocities. Reaction half-lives are requested for all 7 media. The advective residence time selected for air also applies to aerosols and the residence time for water applies to suspended sediment and fish. The advective residence time of aerosols, suspended sediment and fish cannot be specified independently of the air and water residence times.

**Result** : Output

| | Mass% | Half life(hr) | Emissions(kg/hr) |
|---|---|---|---|
| Air | 19.4 | 25.2 | 1000 |
| Water | 61.0 | 360 | 1000 |
| Soil | 19.5 | 720 | 1000 |
| Sediment | 0.1 | 3240 | 0 |

**Test condition** : Physchem Inputs
Molar Mass = 102.18
Data Temperature = 25 ºC
Water Solubility = 8800 mg/l exp.
Vapour Pressure = 19865 Pa exp.
Log Kow = 1.52 exp.
Melting Point = -86.8 ºC exp.

Reaction Half Lives in hours (if not available they can be predicted using EPIWIN)

| | |
|---|---|
| Air (gaseous) | 25.2 |
| Water (no susp. part.) | 360 |
| Bulk Soil | 720 |
| Bulk Sediment | 3240 |
| Suspended Particles | 360 |
| Fish | 360 |
| Aerosol | 25.2 |

Environmental Properties (EQC standard environment)
Dimensions (all defaults)
Densities (all defaults)
Organic carbon & Advection (all defaults)
Transport Velocities (all defaults)

Emission and Inflows (defaults used)
Air 1000 kg/hr
Water 1000 kg/hr
Soil 1000 kg/hr
Sediment 0 kg/hr

**Test substance** : Diisopropyl Ether, CAS No. 108-20-3

**Conclusion** : The majority of DIPE is calculated to partition into the water phase, with smaller but significant amounts into air and soil, based on the modeling parameters used in this calculation. DIPE is considered to be a Type 1 chemical with potential to partition into all environmental compartments.

**Reliability** : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.

**Flag** : Critical study for SIDS endpoint
01.11.2005 (21) (23) (24) (25)

### 3.3.2 DISTRIBUTION

## 3.4 MODE OF DEGRADATION IN ACTUAL USE

## 3.5 BIODEGRADATION

**Type** : aerobic
**Inoculum** : activated sludge, domestic
**Contact time** : 28 day(s)
**Degradation** : (±) % after
**Result** : other: not readily biodegradable
**Deg. product** :
**Method** : OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
**Year** : 1982
**GLP** : no
**Test substance** : other TS: Diisopropyl Ether (CAS No. 108-20-3)

**Result** : Test substance was not readily biodegradable. After 28 days, the test substance exhibited no measurable biodegradation. By day 5, >60% biodegradation of positive control was observed, which meets the guideline requirement. No excursions from the testing guideline were noted. The inhibition study showed that the test substance did not inhibit the biodegradability of the positive control substance, sodium benzoate.

| Sample | % Degradation* Mean (day 28) | % Degradation (day 28) |
|---|---|---|
| Test Substance | 0.0, 0.0 | 0.0 |
| Na Benzoate | 65.0, 73.0 | 69.0 |

* duplicate data

Mean oxygen concentrations (mg/L) of duplicate test systems:

Day 0
Mineral Salts Control = 8.85
Blank = 8.8
Na Benzoate = 8.95
Test Substance = 8.9 (single test system)
Test Substance + Na Benzoate = 8.9* (single test system)

Day 5
Mineral Salts Control = 9.0
Blank = 8.8
Na Benzoate = 5.7
Test Substance = 8..85
Test Substance + Na Benzoate = 5.8

Day 15
Mineral Salts Control = 8.75
Blank = 8.65
Na Benzoate = 4.9
Test Substance = 8.55
Test Substance + Na Benzoate = 4.9

Day 28
Mineral Salts Control = 8.65
Blank = 7.05
Na Benzoate = 3.6
Test Substance = 8.3
Test Substance + Na Benzoate = 4.15

**Test condition** : The inoculum source was the Sittingbourne Sewage works in Kent,

England, and was prepared according to methods described in the OECD 301D guideline. The test substance was added to the test medium by direct addition at a concentration of 3.0 mg/L. Test systems were incubated at 20 ± 1 °C and biodegradation was determined by measuring the oxygen concentration on days 5, 15, and 28. Each sampling of the test substance and control was conducted in duplicate. The theoretical oxygen demand was 2.82 mg O2 per mg test substance and a theoretical carbon dioxide (CO2) evolution of 2.59 mg CO2 per mg test substance. Sodium benzoate was used as the positive control.

The purity of the test substance was not supplied, but the infra-red spectrum of the test substance matched a published standard (density = 0.723 to 0.726 kg/L). The test substance was stored in the dark at ambient temperature. Nitrogen was blown over the surface of the material when the container was opened and exposed to air in order to minimize peroxide formation.

**Conclusion** : Diisopropyl ether is not readily biodegradable and it did not significantly inhibit the biodegradability of the test substance in an inhibition test.

**Reliability** : (1) valid without restriction

07.12.2005 (30)

### 3.6 BOD5, COD OR BOD5/COD RATIO

### 3.7 BIOACCUMULATION

**Species** : other: see remark
**Exposure period** : at 25 °C
**Concentration** :
**BCF** : = 2.95
**Elimination** :
**Method** : other: calculation
**Year** :
**GLP** : no
**Test substance** : other TS: Diisopropyl Ether (CAS # 108-20-3)

**Remark** : A log bioconcentration factor (BCF) of 0.47 is calculated (BCF = 2.95). With respect to a log Kow = 1.52, which was used to calculate the BCF, diisopropyl ether in the aquatic environment is expected to have a low bioaccumulation potential.

**Reliability** : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated and not measured.

**Flag** : Critical study for SIDS endpoint

12.12.2005 (10)

**Species** : other: see remark
**Exposure period** : at 25 °C
**Concentration** :
**BCF** : = 14.06
**Elimination** :
**Method** : other: calculation
**Year** :
**GLP** : no
**Test substance** : other TS: Diisopropyl Ether (CAS No. 108-20-3)

**Remark** : A log bioconcentration factor (BCF) of 1.15 is calculated (BCF = 14.06). With respect to a log Kow = 2.4, which was used to calculate the BCF, disiopropyl ether in the aquatic environment is expected to have a low

bioaccumulation potential.

**Reliability** : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated and not measured.

12.12.2005 (10)

### 3.8 ADDITIONAL REMARKS

## 4.1 ACUTE/PROLONGED TOXICITY TO FISH

| | | |
|---|---|---|
| **Type** | : | flow through |
| **Species** | : | Pimephales promelas (Fish, fresh water) |
| **Exposure period** | : | 96 hour(s) |
| **Unit** | : | mg/l |
| **LC50** | : | = 91.7 |
| **Limit test** | : | |
| **Analytical monitoring** | : | yes |
| **Method** | : | other: Flow-through Fish Acute Toxicity Test |
| **Year** | : | 1983 |
| **GLP** | : | no data |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS No. 108-20-3) |
| **Method** | : | The water solubility of the test chemical was obtained from literature or determined experimentally. A flow through system using proportional diluters and modified continuous mini-diluter system was used for maintaining the required test concentrations<br><br>Twenty to twenty-five 30 day-old fish, each weighing approximately 0.12 g, were randomly divided amongst the test tanks (control and five different concentrations) with flow-through dilutor systems.<br><br>Lake Superior water maintained at 25°C ± 1°C was used in the test. Routine measures of hardness (EDTA) and total alkalinity of test water yielded mean values of 45.5 and 42.2 mg/L as CaCO3, respectively. The arithmetic mean of the pH was 7.5 and dissolved oxygen was always greater than 60% of saturation.<br><br>Fish were supplied from the United States Environmental Protection Agency, Environmental Research Laboratory-Duluth culture. They were not fed during the test. Deaths were recorded after 1, 3, 6,12, 24, 48, 72, and 96 hours. |
| **Remark** | : | Statistics: Trimmed Spearman-Karber Method<br>Test method described in reference. |
| **Result** | : | 96-hour LL50 = 91.7 mg/L based upon measured values<br><br>Analytical method used was GC analysis with Flame Ionization Detection (GC-FID), performed on a Hewlett-Packard model 5730A gas chromatograph. Concentrations of the test chemical were measured daily at each exposure level. |
| **Conclusion** | : | 96-hour LC50 = 91.7 mg/L based upon measured values. |
| **Reliability** | : | (2) valid with restrictions<br>This robust summary has a reliability rating of 2 because complete information on the analytical results were not available and the study was not conducted under GLP. |
| **Flag** | : | Critical study for SIDS endpoint |

01.11.2005 (31)

| | | |
|---|---|---|
| **Type** | : | |
| **Species** | : | other: Fish |
| **Exposure period** | : | 96 hour(s) |
| **Unit** | : | mg/l |
| **LC50** | : | = 214.1 |
| **Method** | : | other: ECOSAR version 0.99h, US EPA |
| **Year** | : | |
| **GLP** | : | |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS No. 108-20-3) |

| | | |
|---|---|---|
| **Method** | : | ECOSAR version 0.99h, US EPA. The structure-activity relationships (SARs) presented in this program are used to predict the aquatic toxicity of chemicals based on their similarity of structure to chemicals for which the aquatic toxicity has been previously measured. Most SAR calculations in the ECOSAR Class Program are based upon the octanol/water partition coefficient (Kow). SARs have been used by the U.S. Environmental Protection Agency since 1981 to predict the aquatic toxicity of new industrial chemicals in the absence of test data. SARs are developed for chemical classes based on measured test data that have been submitted by industry or they are developed by other sources for chemicals with similar structures, e.g., phenols. Using the measured aquatic toxicity values and estimated Kow values, regression equations can be developed for a class of chemicals. Toxicity values for new chemicals may then be calculated by inserting the estimated Kow into the regression equation and correcting the resultant value for the molecular weight of the compound.<br><br>To date, over 150 SARs have been developed for more than 50 chemical classes. These chemical classes range from the very large, e.g., neutral organics, to the very small, e.g., aromatic diazoniums. Some chemical classes have only one SAR, such as acid chlorides, for which only a fish 96-hour LC50 has been developed. The class with the greatest number of SARs is the neutral organics, which has SARs ranging from acute and chronic SARs for fish to a 14-day LC50 for earthworms in artificial soil. The ECOSAR Class Program is a computerized version of the ECOSAR analysis procedures as currently practiced by the Office of Pollution Prevention and Toxics (OPPT). It has been developed within the regulatory constraints of the Toxic Substances Control Act (TSCA). It is a pragmatic approach to SAR as opposed to a theoretical approach. |
| **Result** | : | LC50, 96 h, for fish = 214.1 mg/L |
| **Test condition** | : | Experimental water solubility, 8800 mg/l @ 20°C (Heitmann, W et al, 1987), log Kow, 1.52 (Funasaki, N et al, 1985) and melting point, -86.6°C (SRC PhysProp database) were entered into the program.<br>Class: Neutral organics |
| **Test substance** | : | Diisopropyl Ether (CAS No. 108-20-3) |
| **Conclusion** | : | The predicted 96 h LC50 value for fish (214.1 mg/L) is in good agreement with the experimental 96 h LC50 value for fathead minnow (Pimephales promelas) (91.7 mg/L) (Veith et al., Can. J. Fish. Aquat. Sci., 40:743-748) and 48 h EC50 value for Daphnia (190.0 mg/L) (Stephenson R.R., Shell Research Limited, Report No. SBGR.83.215). |
| **Reliability** | : | (2) valid with restrictions<br>This robust summary has a reliability rating of 2 because the data are calculated and not measured. |

28.10.2005 (9)

| | | |
|---|---|---|
| **Type** | : | flow through |
| **Species** | : | Pimephales promelas (Fish, fresh water) |
| **Exposure period** | : | 96 hour(s) |
| **Unit** | : | mg/l |
| **LC50** | : | = 786 |
| **EC50** | : | = 476 |
| **Limit test** | : | |
| **Analytical monitoring** | : | yes |
| **Method** | : | other: Flow-through Fish Acute Toxicity Test |
| **Year** | : | 1983 |
| **GLP** | : | no data |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS No. 108-20-3) |

| | | |
|---|---|---|
| **Method** | : | Test solutions were prepared using a proportional diluter system without replication. This system provided control and five test substance concentrations to glass test vessels. Each vessel held 2 L of test solution and the diluter flow rate was sufficient to provide 18 volume additions per day. An aqueous stock solution of 1050 mg/L was used by the diluter to |

prepare the exposure series. Dilution water was filtered Lake Superior water. Typical ranges of water quality factors measured in this water were pH (7.4 - 8.2), total hardness (44 - 53 mg/L as CaCO3), and specific conductance (78 - 86 mmhos/cm).

Test fish originated from in-house cultures of P. promelas at the U.S. EPA Environmental Research Laboratory - Duluth. Fish were not fed 24 h prior to testing or during the test. At test initiation, fish were randomly placed in test vessels until each vessel contained 10 individuals. Individuals used in testing were 34 d old and measured 19.0 mm mean length (SD = 2.534) and 0.104 g mean weight (SD = 0.0433). Biomass loading was 1.04 g/L. Death was the major test endpoint. Numbers of dead fish were counted daily and any dead fish were removed from the vessels. Abnormal behavioral changes were recorded at each observation time. LC50 (lethality) and EC50 (total effect) values were determined.

Temperature, dissolved oxygen, and pH were measured daily in all test chambers. Mean values (and Standard Deviation) were 24.9 °C (SD = 0.52), 7.3 mg/L (SD = 0.13), and 7.75 (SD = 0.16), respectively. Total hardness and alkalinity were measured once in the control, low, medium, and high test levels. Mean values were 43.7 mg/L total hardness as CaCO3 (SD = 0.96) and 49.6 mg/L alkalinity as CaCO3 (SD = 0.25). Lighting was provided by fluorescent bulbs that produced 28 to 48 lumens/sq ft at the water surface. The photoperiod was 16 h light and 8 h dark.

Test substance concentrations were verified in most cases daily during the test using gas-liquid chromatography. Concentrations were averaged and a mean percent recovery was calculated. The nominal with measured concentrations in parentheses were, control (not detected), 157 mg/L (131 mg/L), 242 mg/L (210 mg/L), 373 mg/L (382 mg/L), 574 mg/L (594 mg/L), and 883 mg/L (1044 mg/L). The overall percent recovery was 98.7%.

**Remark** : Statistics: LC/EC50 values determined by Trimmed Spearman-Karber Method

**Result** : 96-hour LC50 = 786 mg/L based on mean measured values.
96-hour EC50 = 476 mg/L based on mean measured values.

The EC50 value was based on mortality and the following abnormal effects: loss of schooling behavior, swimming near the surface, hypoactive, under-reactive to external stimuli, loss of equilibrium.

**Conclusion** : 96-hour LC50 = 786 mg/L based on mean measured values.
96-hour EC50 = 476 mg/L based on mean measured values.

**Reliability** : (1) valid without restriction
12.12.2005 (12)

**Type** : flow through
**Species** : Pimephales promelas (Fish, fresh water)
**Exposure period** : 96 hour(s)
**Unit** : mg/l
**LC50** : = 900
**Limit test** :
**Analytical monitoring** : yes
**Method** : other: Flow-through Fish Acute Toxicity Test (ASTM, 1980)
**Year** : 1985
**GLP** : no data
**Test substance** : other TS: Diisopropyl Ether (CAS No. 108-20-3)

**Method** : Test solutions were prepared using a continuous-flow diluter delivery system, which delivered four test substance concentrations and control solutions to duplicate test vessels. Dilution water was filtered Lake Superior water. Average values for water quality factors for the dilution water were: hardness (44.6 mg/L as CaCO3), total alkalinity (44.0 mg/L as

CaCO3), and pH (7.6). Test chambers were glass vessels and contained 2 L of test solution. Solution flow rates through the test chambers was sufficient to provided at least a 95% replacement in approximately 4 h. Test substance concentrations were verified daily during the test using either gas chromatography or high pressure liquid chromatography methods.

The mean temperature for the test was 25 ± 0.5°C, and dissolved oxygen remained at or above 80% saturation. Lighting was provided by wide spectrum fluorescent bulbs at an intensity of 22 to 38 lumens/sq ft over the test chambers. The photoperiod was 16 h light and 8 h dark with a 30-min dusk/dawn transition period.

Test fish originated from cultures maintained by the U.S. EPA Environmental Research Laboratory - Duluth, MN. and were 28 to 34 days old (weighing approximately 0.12 g) at the time of testing. A total of 20 fish per treatment (10/replicate) was used in the test. Fish were added to the test chambers 2-3 h before introduction of the test solutions. Fish were not fed 24 h before or during the test. Mortalities were recorded daily.

**Remark** : Statistics: Trimmed Spearman-Karber Method or log-probit method.
**Result** : 96-h LC50 = 900 mg/L based on measured concentrations
95% CL = 881 - 920 mg/L
**Conclusion** : 96-h LC50 = 900 mg/L based on measured concentrations
**Reliability** : (1) valid without restriction
12.12.2005 (2)

**Type** : static
**Species** : Carassius auratus (Fish, fresh water)
**Exposure period** : 24 hour(s)
**Unit** : mg/l
**LC50** : = 380
**Limit test** :
**Analytical monitoring** : yes
**Method** : other: static acute fish toxicity test (APHA, 1971)
**Year** :
**GLP** : no data
**Test substance** : other TS: Diisopropyl Ether (CAS No. 108-20-3)

**Method** : The test consisted of exposing groups of six fish to a series of concentrations of the test substance for 24 h. Fish were exposed in an all glass tanks holding 25 liters of test solution. Dilution water was local tap water having the following characteristics (all values in mg/L):
$Cl^-$ = 65; $NO2^-$ = 0; $NO3^-$ = 4; $SO4^-2$ = 35; $PO4^-3$ = 0.15; $HCO3^-$ = 25; SiO2 = 25; NH4+ = 0; Fe = 0.05; Mn = 0; Ca+2 = 100; Mg+2 = 8; alkali as Na+ = 30; pH = 7.8.

The test was run at a temperature of 20±1°C, and the solutions were not aerated during the test period.

Test fish had a mean length of 6.2±0.7 cm, a mean weight of 3.3 ± 1.0 g and were in good health at the time of testing.

Exposure concentrations were confirmed either by total organic carbon analysis or by extraction and subsequent analysis by gas chromatography. Measured concentrations were not reported in this study.

**Remark** : Determination of LC50 by graphical interpolation of log concentrations versus percent mortality (APHA, 1971).
**Result** : 24-hour LC50 = 380 mg/L

The analytical method was either total organic carbon analysis or gas chromatography. It was not reported what method was employed for this test substance nor if the result was based on measured concentrations.

| | | |
|---|---|---|
| **Conclusion** | : | 24-hour LC50 = 380 mg/L. |
| **Reliability** | : | (3) invalid<br>The test was run for only 24 hours to ensure that the dissolved oxygen content did not fall below 4 mg/L. The report lacked sufficient detail for assessment. It was not stated whether results were based on nominal or measured values. |

12.12.2005 (1)

| | | |
|---|---|---|
| **Type** | : | static |
| **Species** | : | Lepomis macrochirus (Fish, fresh water) |
| **Exposure period** | : | 96 hour(s) |
| **Unit** | : | mg/l |
| **LC50** | : | 7000 |
| **Limit test** | : | |
| **Analytical monitoring** | : | no |
| **Method** | : | other: static acute fish toxicity test |
| **Year** | : | |
| **GLP** | : | no |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS No. 108-20-3) |

**Method** : The test consisted of exposing groups of fish to a four-dilution series of the test substance for a period of 96 h. Test vessels were all glass 5-gallon aquaria. The volume of test solution was adjusted to assure that a biomass loading was no more than 1 g fish /liter solution. Dilution water was well water having a typical pH of 7.6 to 7.9 and a hardness of 55 mg/L (as CaCO3).

Fish were obtained from a commercial source and assessed for health during a 14-d acclimation period prior to testing. During that time they were maintained on a commercial fish food diet supplemented with minced frozen shrimp. Fish were not fed 48 hours prior to testing. Fish were randomly selected for testing and were approximately 33 to 75 mm in length.

The test was run at 23°C. Test solutions were not aerated for the initial 24 h, but aeration was applied thereafter if the dissolved oxygen concentration was being depleted. Dissolved oxygen readings were taken daily, and pH was measured at the end of the test. However, these data were not provided in the report.

Mortality was assessed daily and any dead fish were removed at each observation time.

**Remark** : The LC50 was determined by plotting survival percentages on semi-logarithmic paper and drawing a straight line fit through or near significant points above and below 50% survival.

**Result** : 96-hour LC50 = 7,000 mg/L

The mortality pattern reported for the test substance suggests that a more likely estimate of the LC50 value would lie between 7,900 and 10,000 mg/L, rather than 7,000 mg/L. This was due to a non-monotonic dose response pattern of mortality. The report authors indicated that the LC50 value was higher than the published solubility for the test substance.

| | | |
|---|---|---|
| **Conclusion** | : | 96-hour LC50 = 7,000 mg/L based on nominal concentrations |
| **Reliability** | : | (3) invalid<br>Documentation was insufficient for evaluation. Basic water quality data during the test were not provided. The authors stated that aeration of the test solutions was used after 24 hours to ensure maintenance of dissolved oxygen. No analytical verification of exposure concentrations were made. |

12.12.2005 (7)

| | | |
|---|---|---|
| **Type** | : | static |
| **Species** | : | Menidia beryllina (Fish, estuary, marine) |

| | | |
|---|---|---|
| **Exposure period** | : | 96 hour(s) |
| **Unit** | : | mg/l |
| **LC50** | : | 6600 |
| **Limit test** | : | |
| **Analytical monitoring** | : | no |
| **Method** | : | other: static acute fish toxicity test |
| **Year** | : | |
| **GLP** | : | no |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS No. 108-20-3) |

**Method** : The test consisted of exposing groups of fish to a four-dilution series of the test substance for a period of 96 h. Test vessels were all glass 5-gallon aquaria. The volume of test solution was adjusted to assure that a biomass loading was no more than 1 g fish /liter solution. Dilution water was prepared by adding "instant ocean" salts to well water (pH of 7.6 to 7.9; hardness 55 mg/L (as CaCO3)) until a specific gravity of 1.018 was achieved.

Fish were field collected in nets from Horseshoe Bay at Sandy Hook, New Jersey. They were held for a 14-d acclimation period prior to testing and assessed for health during that time. During the acclimation period they were fed minced frozen shrimp. Fish were not fed 48 hours prior to testing. Fish were randomly selected for testing and were approximately 40 to 100 mm in length.

The test was run at 20°C, and test solutions were continuously aerated during the exposure period. Dissolved oxygen readings were taken daily, and pH was measured at the end of the test. However, these data were not provided in the report.

Mortality was assessed daily and any dead fish were removed at each observation time.

**Remark** : LC50 determined by graphical interpolation of the logarithm of the concentration versus the percentage mortality.

**Result** : 96-hour LC50 = 6600 mg/L

The mortality pattern reported for the test substance does not correspond with the estimated LC50 value. Given the dose-response pattern, the LC50 value would lie between 3,200 and 5,000 mg/L, rather than 6,600 mg/L. The authors reported that the result was higher than the reported water solubility of the test substance.

**Conclusion** : 96-hour LC50 = 6600 mg/L based on nominal concentrations.

**Reliability** : (3) invalid
Documentation was insufficient for evaluation. Basic water quality data during the test were not provided. The authors stated that aeration of the test solutions was used after 24 hours to ensure maintenance of dissolved oxygen. No analytical verification of exposure concentrations were made.

12.12.2005 (7)

## 4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

| | | |
|---|---|---|
| **Type** | : | |
| **Species** | : | Daphnia magna (Crustacea) |
| **Exposure period** | : | 48 hour(s) |
| **Unit** | : | mg/l |
| **EC50** | : | = 190 |
| **Analytical monitoring** | : | no |
| **Method** | : | other: U.S. Environmental Protection Agency, Methods for acute toxicity testing with fish, macro-invertebrates and amphibians (EPA-660/3-75-009) |
| **Year** | : | 1975 |

**GLP** : no
**Test substance** : other TS: Diisopropyl Ether (CAS No. 108-20-3)

**Remark** : Statistics:
Probit analysis after log transformation of the concentrations (Finney, 1971)
Probit Analysis, Finney, D.J., Cambridge University Press, 3rd edition, p333 (1971)

**Result** : The 24 h and 48 h Effect Concentration (EC50) values were calculated to be 240 mg/L (95% fiducial limits 210 to 280 mg/L) and 190 mg/L (95% fiducial limits 160 to 220 mg/L), respectively.
The immobilization (%) of Daphnia magna (n=10/replicate) are as follows:

| Test Substance Loading Rate (mg/L) | Immobilization (%)* 24 hr | 48 hr |
|---|---|---|
| 0 (control) | 0 | 0 |
| 46 | 0 | 0 |
| 99 | 3 | 7 |
| 210 | 27 | 57 |
| 460 | 100 | 100 |
| 1000 | 100 | 100 |

*mean of 3 replicates

**Test condition** : A 48 hour static toxicity test was carried out without renewal of the test solutions. Quantities of stock solutions of di-isopropyl ether in acetone were added in triplicate sets of 110 mL glass flasks so that when made up with reconstituted freshwater, an approximately logarithmic series of concentrations ranging from 46 to 1000 mg/L was produced. Three flasks served as controls and received no test substance. The concentration of acetone in all control and test flasks was 0.1 mL/L. Precautions were taken to (a) minimise evaporative loss of the test substance by use of glass cover slips over the vessel necks and (b) to minimize the risk of organisms becoming trapped at the surface by placing black paper caps over the flasks to create a darkened zone which the organisms would avoid.
The test temperatures were in the range 20 ± 2°C, pH was in the range 8.2 to 8.4, the total hardness was 164 mg/L as CaCO3, and dissolved oxygen was in the range 8.2 to 9.2 mg/L.
The daphnids were cultured in-house, derived from a strain obtained (via ICI Brixham Laboratory) from Institut National de Recherche Chimique Applique (I.R.Ch.A.), France. Age was <24 hours old from 15 to 35 day old parents.
All concentrations of test substance are expressed in terms of quantities initially added to the test vessels.

**Test substance** : Diisopropyl Ether (CAS No. 108-20-3)
**Conclusion** : After Daphnia magna were exposed to test solutions of di-isopropyl ether for 48 hours in a static test, the 24 h and 48 h EC50 values were calculated to be 240 mg/L and 190 mg/L, respectively.
**Reliability** : (2) valid with restrictions
This robust summary has a reliability rating of 2 because it did not analytically verify exposure concentrations and the results are based on nominal values.

07.12.2005 (28)

**Type** :
**Species** : other: Daphnia
**Exposure period** : 48 hour(s)
**Unit** : mg/l
**EC50** : = 221.9
**Method** : other: ECOSAR version 0.99h, US EPA
**Year** :
**GLP** :
**Test substance** : other TS: Diisopropyl Ether (CAS No. 108-20-3)

| | | |
|---|---|---|
| **Method** | : | ECOSAR version 0.99h, US EPA. The structure-activity relationships (SARs) presented in this program are used to predict the aquatic toxicity of chemicals based on their similarity of structure to chemicals for which the aquatic toxicity has been previously measured. Most SAR calculations in the ECOSAR Class Program are based upon the octanol/water partition coefficient (Kow). SARs have been used by the U.S. Environmental Protection Agency since 1981 to predict the aquatic toxicity of new industrial chemicals in the absence of test data. SARs are developed for chemical classes based on measured test data that have been submitted by industry or they are developed by other sources for chemicals with similar structures, e.g., phenols. Using the measured aquatic toxicity values and estimated Kow values, regression equations can be developed for a class of chemicals. Toxicity values for new chemicals may then be calculated by inserting the estimated Kow into the regression equation and correcting the resultant value for the molecular weight of the compound.<br><br>To date, over 150 SARs have been developed for more than 50 chemical classes. These chemical classes range from the very large, e.g., neutral organics, to the very small, e.g., aromatic diazoniums. Some chemical classes have only one SAR, such as acid chlorides, for which only a fish 96-hour LC50 has been developed. The class with the greatest number of SARs is the neutral organics, which has SARs ranging from acute and chronic SARs for fish to a 14-day LC50 for earthworms in artificial soil. The ECOSAR Class Program is a computerized version of the ECOSAR analysis procedures as currently practiced by the Office of Pollution Prevention and Toxics (OPPT). It has been developed within the regulatory constraints of the Toxic Substances Control Act (TSCA). It is a pragmatic approach to SAR as opposed to a theoretical approach. |
| **Result** | : | EC50, 48 h, for Daphnia = 221.9 mg/L |
| **Test condition** | : | Experimental water solubility, 8800 mg/l @ 20°C (Heitmann, W et al, 1987), log Kow, 1.52 (Funasaki, N et al, 1985) and melting point, -86.6°C (SRC PhysProp database) were entered into the program.<br>Class: Neutral organics |
| **Test substance** | : | Diisopropyl Ether, CAS No. 108-20-3 |
| **Conclusion** | : | The predicted 48 h LC50 value for Daphnia (221.9 mg/L) is in close agreement with the experimental 48 h EC50 value for Daphnia (190.0 mg/L) (Stephenson R.R., Shell Research Limited, Report No. SBGR.83.215). |
| **Reliability** | : | (2) valid with restrictions<br>This robust summary has a reliability rating of 2 because the data are calculated and not measured. |

28.10.2005 (9)

### 4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

| | | |
|---|---|---|
| **Species** | : | other algae: Green Alga |
| **Endpoint** | : | |
| **Exposure period** | : | 96 hour(s) |
| **Unit** | : | mg/l |
| **EC50** | : | = 134.9 |
| **ChV** | : | = 10.2 |
| **Method** | : | other: ECOSAR version 0.99h, US EPA |
| **Year** | : | |
| **GLP** | : | |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS No. 108-20-3) |
| **Method** | : | ECOSAR version 0.99h, US EPA. The structure-activity relationships (SARs) presented in this program are used to predict the aquatic toxicity of chemicals based on their similarity of structure to chemicals for which the |

aquatic toxicity has been previously measured. Most SAR calculations in the ECOSAR Class Program are based upon the octanol/water partition coefficient (Kow). SARs have been used by the U.S. Environmental Protection Agency since 1981 to predict the aquatic toxicity of new industrial chemicals in the absence of test data. SARs are developed for chemical classes based on measured test data that have been submitted by industry or they are developed by other sources for chemicals with similar structures, e.g., phenols. Using the measured aquatic toxicity values and estimated Kow values, regression equations can be developed for a class of chemicals. Toxicity values for new chemicals may then be calculated by inserting the estimated Kow into the regression equation and correcting the resultant value for the molecular weight of the compound.

To date, over 150 SARs have been developed for more than 50 chemical classes. These chemical classes range from the very large, e.g., neutral organics, to the very small, e.g., aromatic diazoniums. Some chemical classes have only one SAR, such as acid chlorides, for which only a fish 96-hour LC50 has been developed. The class with the greatest number of SARs is the neutral organics, which has SARs ranging from acute and chronic SARs for fish to a 14-day LC50 for earthworms in artificial soil. The ECOSAR Class Program is a computerized version of the ECOSAR analysis procedures as currently practiced by the Office of Pollution Prevention and Toxics (OPPT). It has been developed within the regulatory constraints of the Toxic Substances Control Act (TSCA). It is a pragmatic approach to SAR as opposed to a theoretical approach.

**Result** : EC50, 96 h, for green algae = 134.9 mg/L

ChV, 96 h, for green algae = 10.2 mg/L

**Test condition** : Experimental water solubility, 8800 mg/l @ 20°C (Heitmann, W et al, 1987), log Kow, 1.52 (Funasaki, N et al, 1985) and melting point, -86.6°C (SRC PhysProp database) were entered into the program.
Class: Neutral organics

**Test substance** : Diisopropyl Ether (CAS No. 108-20-3)

**Conclusion** : The predicted 96 h EC50 value for algae (134.9 mg/L) is in the same range as the predicted 48 h LC50 value for Daphnia (221.9 mg/L) and the predicted 96 h LC50 value for fish (214.1 mg/L). There is also good comparison between the predicted and experimental EC50 values for Daphnia (221.9 mg/l v 190.0 mg/L, respectively) and for fish (214.1 mg/l v 91.7 mg/L, respectively).

**Reliability** : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated and not measured.

28.10.2005 (9)

**Species** : Selenastrum capricornutum (Algae)
**Endpoint** : biomass
**Exposure period** : 96 hour(s)
**Unit** : mg/l
**EC50** : >= 1000
**Limit test** :
**Analytical monitoring** : no
**Method** : other: algae growth inhibition
**Year** : 1983
**GLP** : no data
**Test substance** : other TS: Diisopropyl Ether (CAS No. 108-20-3)

**Method** : A 4 d algal growth study was carried out using 10 concentrations of the test substance and a control. The test design included six control replicates and single vessels dosed with different concentrations of the test substance. 250-mL glass Erlenmeyer flasks served as the test vessels and held 50 mL of culture medium. Culture medium was prepare following the recipe given by Miller and Green (1978) with the following exceptions; 1)

boric acid concentration = 105 mg/L, and 2) sodium bicarbonate concentration = 50 mg/L.

To 10 flasks, quantities of a test substance stock solution made up in acetone were added to give a logarithmic series of concentrations ranging from 1 to 1000 mg/L (1.0, 2.2, 4.6, 10, 22, 46, 100, 220, 460, and 1000 mg/L). The concentration of acetone in all flasks including controls was adjusted to 0.1 mL/L. Each flask was inoculated with S. capricornutum to give an initial cell density of 5 x 102 cells/mL. The algal inoculum was prepared from an actively growing liquid culture of S. capricornutum in exponential growth phase.

Flasks were incubated in a temperature controlled orbital incubator under constant illumination (approximately 3000 lux) at 24±2°C for 4 days. Cell counts were made on days 2 and 4 using an electronic particle counter (Coulter counter). The temperature in the incubator was measured at 4-h intervals. The pH of the control and highest test concentration was measured on days 0, 2, and 4. Temperature remained within the 24±2°C specified range, and the pH ranged from 8.3 to 8.5 in the measured vessels.

All determination of EC50 values were based on nominal test concentrations and cell counts.

**Result** : 96-hour EC50 = >1000 mg/L based on nominal concentrations.

The 96-hour cell counts in the treated flasks as a percent of the mean control cell counts were:

| | |
|---|---|
| 1.0 mg/L = 84% | 46 mg/L = 127% |
| 2.2 mg/L = 108% | 100 mg/L = 130% |
| 4.6 mg/L = 91% | 220 mg/L = 113% |
| 10 mg/L = 122% | 460 mg/L = 127% |
| 22 mg/L = 129% | 1000 mg/L = 91% |

**Conclusion** : 96-hour EC50 = >1000 mg/L based on nominal concentrations.

**Reliability** : (3) invalid
Test concentrations were not measured and there is no indication in the report whether the test vessels were sealed. The reported LC50 value may reflect a loss of test substance by volatilization if the flasks were not tightly sealed.

12.12.2005 (29)

## 4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

## 4.5.1 CHRONIC TOXICITY TO FISH

## 4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

## 4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

## 4.6.2 TOXICITY TO TERRESTRIAL PLANTS

## 4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

### 4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

### 4.7 BIOLOGICAL EFFECTS MONITORING

### 4.8 BIOTRANSFORMATION AND KINETICS

### 4.9 ADDITIONAL REMARKS

## 5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

### 5.1.1 ACUTE ORAL TOXICITY

| | | |
|---|---|---|
| **Type** | : | LD50 |
| **Value** | : | |
| **Species** | : | rat |
| **Strain** | : | Sprague-Dawley |
| **Sex** | : | male/female |
| **Number of animals** | : | |
| **Vehicle** | : | other: None; administered undiluted |
| **Doses** | : | |
| **Method** | : | other: Similar to OECD 401 |
| **Year** | : | |
| **GLP** | : | no |
| **Test substance** | : | other TS: Diisopropyl ether (CAS No. 108-20-3) |
| **Method** | : | Administered orally to nonfasted rats. LD50 calculated by the method of Litchfield and Wilcoxon [1949]. Similar to OECD 401. |
| **Remark** | : | Test type: Acute oral toxicity<br>Year: Prior to 1971<br>No. of animals/dose: 6 male for young adult and older adult<br>6 - 12 male and female for 14-day old rats<br>Route of administration: Oral gavage<br>Dose level: Variable<br>Dose volume: Variable<br>Control group included: No, but none needed |
| **Result** | : | 14-day old: LD50 6.4 ml/kg [approx 4.5 g/kg]<br>young adults: LD50 16.5 ml/kg [approx 11.6 g/kg]<br>Older adults: LD50 16.0 ml/kg [approx 11.2 g/kg]<br><br>G/kg dose based on a density of 0.72 g/ml |
| **Test condition** | : | Rats were observed for up to 7 days after dosing. |
| **Test substance** | : | Diisopropyl ether (CAS No. 108-20-3)<br>Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-<br>Source/purity of test material is not specified, but stated to be analytical grade meeting ACS specifications. |
| **Conclusion** | : | DIPE, when administered to adult male Sprague-Dawley rats, had an acute oral LD50 of >10 g/kg. 14-day immature rats were considerable more sensitive [LD50 4.5 g/kg]. |
| **Reliability** | : | (2) valid with restrictions<br>Not GLP but conducted at a reputable laboratory [Abbot Laboratories, Chicago]. |

01.11.2005 (18)

| | | |
|---|---|---|
| **Type** | : | |
| **Value** | : | |
| **Species** | : | rabbit |
| **Strain** | : | New Zealand white |
| **Sex** | : | no data |
| **Number of animals** | : | 6 |
| **Vehicle** | : | other: none reported |
| **Doses** | : | 8.2, 7.2, 6.0, 5.2, 3.3, 1.62 g/kg |
| **Method** | : | other: Similar to OECD 401 |
| **Year** | : | |
| **GLP** | : | no |

| | | |
|---|---|---|
| **Test substance** | : | other TS: Diisopropyl ether (CAS No. 108-20-3) |
| **Remark** | : | Test type: Acute oral toxicity<br>Year: Prior to 1939<br>Route of administration: Oral<br>Dose levels: 8.2, 7.2, 6.0, 5.2, 3.3, 1.62 g/kg<br>Dose volume: Variable<br>Control: No - none needed |
| **Result** | : | Minimal lethal dose between 7 - 9 ml/kg<br><br>The symptoms noted were lack of coordination and unsteadiness at onset followed by a slight narcosis. In the animals that died the narcosis progressed towards a deep narcosis with loss of corneal reflex and evidences of depressant action on the medulla appeared, respiration became progressively slower, irregular and variable in amplitude and drop in body temperature till respiration failed. In the surviving animals, no effect on HB, erythrocyte count, total and differential leukocyte count was observed. No delayed toxicity was observed during the recovery period of 4 months after treatment. |
| **Test substance** | : | Diisopropyl ether (CAS No. 108-20-3)<br>Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-<br>Test material is stated to be commercial grade with 3% of isopropyl alcohol, but with no peroxide nor added inhibitor. |
| **Conclusion** | : | The test article, when administered orally as received to New Zealand white rabbits had a minimal lethal dose of 7 - 9 ml/kg [approx 5 - 6.5 g/kg]. |
| **Reliability** | : | (2) valid with restrictions<br>Not conducted by GLP but at a reputable laboratory [Kettering Laboratory, University of Cincinnati]. |

01.11.2005 (20)

### 5.1.2 ACUTE INHALATION TOXICITY

| | | |
|---|---|---|
| **Type** | : | |
| **Value** | : | |
| **Species** | : | guinea pig |
| **Strain** | : | other: not specified |
| **Sex** | : | no data |
| **Number of animals** | : | |
| **Vehicle** | : | other: none |
| **Doses** | : | 0.3%; 1%; 3%; 6% in air |
| **Exposure time** | : | |
| **Method** | : | other: not specified |
| **Year** | : | |
| **GLP** | : | no |
| **Test substance** | : | other TS: Diisopropyl ether (CAS No. 108-20-3) |
| **Remark** | : | Test type: Acute inhalation toxicity<br>Year: Prior to 1939<br>No. animlas/sex/group: One to two animals per dose<br>Route of administration: Inhalation<br>Dose level: 0.3%; 1%; 3%; 6% in air<br>Dose volume: N/A<br>Control: No |
| **Result** | : | 0.3 % (~3000 ppm)- 2 h: No visible indication of anesthetic action<br>1 and 3.0 % (~30000 ppm)- 1 h: Not lethal; signs of anesthesia<br>6.0% (~60000 ppm) : Death as the result of respiratory failure within 1 hr |
| **Test condition** | : | 1 or 2 hrs or until death [6%] |
| **Test substance** | : | Diisopropyl ether (CAS No. 108-20-3)<br>Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], |

2,2 '-
Test material is stated to be commercial grade with 3% of isopropyl alcohol, but with no peroxide or added inhibitor.

**Conclusion** : The lowest lethal dose for 1 hr exposure was greater than 30,000 ppm in three species.

**Reliability** : (2) valid with restrictions
Not conducted by GLP. Few animals per group, but at a reputable laboratory [Kettering Laboratory, University of Cincinnati].

01.11.2005 (20)

**Type** :
**Value** :
**Species** : rabbit
**Strain** : New Zealand white
**Sex** : no data
**Number of animals** :
**Vehicle** : other: none
**Doses** : 0.3%; 1%; 3%; 6% in air
**Exposure time** :
**Method** : other: not specified
**Year** :
**GLP** : no
**Test substance** : other TS: Diisopropyl ether (CAS No. 108-20-3)

**Remark** : Test type: Acute inhalation toxicity
Year: Prior to 1939
No. animlas/sex/group: One to two animals per dose
Route of administration: Inhalation
Dose level: 0.3%; 1%; 3%; 6% in air
Dose volume: N/A
Control: No

**Result** : 0.3 % (~3000 ppm)- 2 h: No visible indication of anesthetic action
1 and 3.0 % (~30000 ppm)- 1 h: Not lethal; signs of anesthesia
6.0% (~60000 ppm) : Death as the result of respiratory failure within 1 hr

**Test condition** : 1 or 2 hrs or until death [6%]

**Test substance** : Diisopropyl ether (CAS No. 108-20-3)
Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Test material is stated to be commercial grade with 3% of isopropyl alcohol, but with no peroxide or added inhibitor.

**Conclusion** : The lowest lethal dose for 1 hr exposure was greater than 30,000 ppm in three species.

**Reliability** : (2) valid with restrictions
Not conducted by GLP. Few animals per group, but at a reputable laboratory [Kettering Laboratory, University of Cincinnati].

01.11.2005 (20)

**Type** :
**Value** :
**Species** : monkey
**Strain** : other: Macacus rhesus
**Sex** : female
**Number of animals** :
**Vehicle** : other: none
**Doses** : 0.3%; 1%; 3%; 6% in air
**Exposure time** :
**Method** : other: not specified
**Year** :
**GLP** : no
**Test substance** : other TS: Diisopropyl ether (CAS No. 108-20-3)

**Remark** : Test type: Acute inhalation toxicity

Year: Prior to 1939
No. animlas/sex/group: One to two animals per dose
Route of administration: Inhalation
Dose level: 0.3%; 1%; 3%; 6% in air
Dose volume: N/A
Control: No

**Result** : 0.3 % (~3000 ppm)- 2 h: No visible indication of anesthetic action
1 and 3.0 % (~30000 ppm)- 1 h: Not lethal; signs of anesthesia
6.0% (~60000 ppm) : Death as the result of respiratory failure within 1 hr

**Test condition** : 1 or 2 hrs or until death [6%]

**Test substance** : Diisopropyl ether (CAS No. 108-20-3)
Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Test material is stated to be commercial grade with 3% of isopropyl alcohol, but with no peroxide or added inhibitor.

**Conclusion** : The lowest lethal dose for 1 hr exposure was greater than 30,000 ppm in three species.

**Reliability** : (2) valid with restrictions
Not conducted by GLP. Few animals per group, but at a reputable laboratory [Kettering Laboratory, University of Cincinnati].

01.11.2005 (20)

### 5.1.3 ACUTE DERMAL TOXICITY

**Type** : LD50
**Value** :
**Species** : rabbit
**Strain** : New Zealand white
**Sex** : no data
**Number of animals** :
**Vehicle** : other: none
**Doses** : variable
**Method** : other: Similar to OECD 402
**Year** :
**GLP** : no
**Test substance** : other TS: Diisopropyl ether (CAS No. 108-20-3)

**Remark** : Test type: Acute dermal toxicity
Year: Prior to 1939
No. of animals/sex/group: Unspecified
Route of administration: Dermal
Dose level: variable
Control: No

**Result** : No deaths or systemic effects were reported. In rabbits dermal unoccluded LD50 > 2.0 g/kg. The actual dose applied was much higher, but continued to evaporate from the skin during application.

**Test condition** : The material was continuously dripped onto the shaved skin to keep it wet for one hour, while continuously evaporating. 150 ml of material was used.

**Test substance** : Diisopropyl ether (CAS No. 108-20-3)
Chemical Name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Test material is stated to be commercial grade with 3% of isopropyl alcohol, but with no peroxide or added inhibitor.

**Conclusion** : The test article, when administered dermally to New Zealand white rabbits had an acute dermal LD50 of greater than 2.0 g/kg.

**Reliability** : (2) valid with restrictions
Not GLP but conducted at a reputable laboratory [Kettering Laboratory, University of Cincinnati].

01.11.2005 (20)

### 5.1.4 ACUTE TOXICITY, OTHER ROUTES

### 5.2.1 SKIN IRRITATION

### 5.2.2 EYE IRRITATION

### 5.3 SENSITIZATION

| | | |
|---|---|---|
| **Type** | : | other: In vitro chemical reactivity assay, surrogate for respiratory sensitization |
| **Species** | : | other: No animals; in vitro chemical assay |
| **Number of animals** | : | 0 |
| **Vehicle** | : | other: None |
| **Result** | : | not sensitizing |
| **Classification** | : | not sensitizing |
| **Method** | : | other: No guideline available |
| **Year** | : | 1990 |
| **GLP** | : | no |
| **Test substance** | : | other TS: Diisopropyl ether (CAS No.108-20-3) |
| **Remark** | : | Route of administration: N/A<br>Sex: N/A<br>Dose level: N/A<br>Dose volume: N/A<br>Control group included: Positive and negative controls included |
| **Result** | : | Diisopropanol was negative in this in vitro assay for potential respiratory sensitization. The assay gave positive responses with several known respiratory sensitizers. |
| **Test condition** | : | A method for monitoring chemical reactivity in aqueous solutions, at neutral pH and 37 degrees C, was developed. The chemical was allowed to react with a lysine-containing peptide, and the reaction was monitored with high-performance liquid chromatography. Simple acids, bases, and solvents did not react with the peptide, whereas isocyanates, anhydrides, and chloramine-T, substances well known for their sensitizing and asthma inducing properties, did. Thus a positive test strongly suggested that the chemical had the potential to act as a hapten and cause sensitization when inhaled. |
| **Test substance** | : | Diisopropyl ether (CAS No.108-20-3)<br>Chemical Name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-<br>Source/purity not specified. |
| **Conclusion** | : | Di-isopropanol was negative in this in vitro assay. |
| **Reliability** | : | (2) valid with restrictions<br>Not conducted by GLP; research method not accepted by regulatory agencies; in vitro surrogate for respiratory sensitisation. |

01.11.2005 (32)

### 5.4 REPEATED DOSE TOXICITY

| | | |
|---|---|---|
| **Type** | : | Sub-chronic |
| **Species** | : | rat |
| **Sex** | : | male/female |
| **Strain** | : | Sprague-Dawley |
| **Route of admin.** | : | inhalation |

| | | |
|---|---|---|
| **Exposure period** | : | 6 hours/day |
| **Frequency of treatm.** | : | 5 days/week for ~13 weeks |
| **Post exposure period** | : | |
| **Doses** | : | 0, 480, 3300, or 7100 ppm |
| **Control group** | : | other: yes (untreated & sham-exposed) |
| **NOAEL** | : | = 480 ppm |
| **Method** | : | EPA OTS 798.2450 |
| **Year** | : | 1996 |
| **GLP** | : | no data |
| **Test substance** | : | other TS: Diisopropyl Ether (CAS No. 108-20-3) |

**Method** : Statistical method:
Statistical analyses of numerical data included ANOVA and Tukey's studentized range test for data on serum chemistry. Duncan's multiple range test was used for hematology and body weights to assess statistically significant differences between control and exposed groups.

**Remark** : Male and female rats were acclimated for 2 weeks before initiation of exposures that began at ~8 weeks of age. Exposed animals were individually housed in 1-m3 inhalation chambers. Untreated control animals were housed in a separate room in identical caging. Room environment was set to 20-22ºC and 40-60% relative humidity. Lights were on a 12/12-hr light/dark cycle. Food and water were provided ad libitum except during exposures.

Vapors were generated by metering DIPE on to a warmed fiberglass wick and carried to the three 1m3 exposure chambers by a stream of measured and filtered room air. Temperature and humidity in the chambers were measured every 30 minutes and air flow through each chamber was metered to provide at least 12 air changes/hour. Chamber air samples were collected with a gas-tight syringe and analyzed with a gas chromatograph with a flame ionization detector and a fused silica column. Samples were periodically obtained for analysis by gas chromatography/ mass spectroscopy.

The primary endpoints during the course of exposures were individual body weights recorded weekly and clinical signs recorded daily except on weekends.

Following the last exposure, rats were fasted overnight and weighed; blood samples were obtained via the orbital sinus using light anesthesia. Samples were used to determine values for WBC, RBC, Hgb, Hct, MCV, MCH, MCHC, platelets, and differential counts. Glucose, urea nitrogen, total protein, albumin, globulin, A/G ratio, sorbitol dehydrogenase, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total bilirubin, creatinine, cholesterol, triglycerides, uric acid, Cl, Ca, Na, K, and P. Following the collection of blood samples, all animals were euthanized with sodium pentobarbital (i.p.) and exanguinated. Approximately 40 tissues were collected for histopathology and organs were weighed. Testis and associated tissues were preserved whole in 10% buffered formalin except for the left cauda epididymis of 10 rats in both control groups and the highest test group; epididymides were evaluated for morphology and number of sperm. The left testis in these groups was weighed and used for determination of number of testicular spermatids.

Type: 90-Day Subchronic
Species/strain: Rat/Sprague-Dawley; Tac:N(SD)fBR
No./sex/dose: 14/sex/group
Vehicle: None
Method: USEPA 1984, 40CFR Part 798:2450

**Result** : DIPE did not adversely affect clinical signs body weight, serum chemistry, hematology, or the number of sperm or spermatids. Exposure to males at

7100 ppm resulted in hypertrophy of liver cells associated with increased liver weight and in increased kidney weight with an increased incidence of hyaline droplets in proximal tubules of the kidney. Females had increased weight of both liver and kidney, although kidney increased only in relation to sham-exposed controls and no morphologic changes were observed in either organ. At 3300 ppm, weights of liver and kidney were increased in males; the liver weights were increased in females only compared to sham-exposed controls and not untreated controls. No morphologic abnormalities were observed. No changes were observed with 480 ppm.

**Test substance** : Diisopropyl Ether (CAS No. 108-20-3); purity ~92%.
**Conclusion** : NOAEL = 480 ppm
**Reliability** : (2) valid with restrictions
GLP unknown. Study well documented, meets generally accepted scientific principles, acceptable for assessment.

01.11.2005 (5)

**Type** : Sub-chronic
**Species** : rat
**Sex** : male/female
**Strain** : Sprague-Dawley
**Route of admin.** : inhalation
**Exposure period** : 6 hours/day
**Frequency of treatm.** : 5 days/week for ~13 weeks
**Post exposure period** :
**Doses** : 0, 450, 3250, or 7060 ppm
**Control group** : other: yes (sham-exposed)
**Method** : other: USEPA 1984, 40CFR Part 798:6050, 6400, and 6200
**Year** : 1997
**GLP** : no data
**Test substance** : other TS: Diisopropyl Ether (CAS No. 108-20-3)

**Method** : Statistical method:
All statistical analyses were performed with SAS software. Body weights, rectal temperatures fore- and hindlimb grip strengths, the number of rears, and motor activity were analyzed by a one-way analysis of variance followed by Duncan's multiple range test. The remaining data from the FOB were analyzed by Fisher's exact test using an extended contingency table containing all four groups of at given sex at a specified time. If a significant difference occurred for a given parameter, Fisher's exact test was used to directly compare each group individually against the control. Brain weights, lengths and widths, were analyzed by Student's t-test.

**Remark** : Male and female rats were acclimated for 2 weeks before initiation of exposures that began at ~8 weeks of age. Sham-exposed and exposed animals were individually housed in 1-m3 inhalation chambers except during behavioral testing, when they were placed in another room overnight and evaluated the following day. Room environment was set to 20-22ºC and 40-60% relative humidity. Lights were on a 12/12-hr light/dark cycle. Food and water were provided ad libitum except during exposures. Exposure vapors were generated by metering DIPE on to a warmed fiberglass wick and carried to the three 1-m3 exposure chambers by a stream of measured and filtered room air. Temperature and humidity in the chambers were measured every 30 minutes and air flow through each chamber was metered to provide at least 12 air changes/hour. Chamber air samples were collected with a gas-tight syringe and analyzed with a gas chromatograph with a flame ionization detector and a fused silica column. Samples were periodically obtained for analysis by gas chromatography/ mass spectroscopy.

Exposures were stagger-started over a 5-day period with 16 animals, 2/sex/group, receiving their first exposure on each of 5 consecutive days.

The rats were observed for signs of toxicity daily prior to initiation of

exposures, and individual body weights were recorded weekly.

During weeks of Functional Observation Battery (FOB) evaluation, four rats/group would be removed from the inhalation chamber and housed separately overnight and evaluated on the following day between the hours of 7:30 a.m. and 11:00 a.m. The process was repeated for each consecutive day until all rats were evaluated. The rats were evaluated with minimal disruption to the exposure schedule and with a manageable number of rats per day, 16 on any given day. The animals were evaluated in an FOB followed by a determination of motor activity prior to initiation of exposure; the FOB following 2, 4, 8, and 13 weeks of exposures, and for motor activity following 4, 8, and 13 weeks of exposures. Following the final determination of motor activity, the animals were anesthetized, intravascularly perfused, and the brain, spinal cord, and peripheral nerves removed for microscopic examination.

The FOB consisted of initially observing home-cage positioning, posture, and reaction to removal from the cage. This was followed by evaluation for exophthalmus/palpebral closure, lacrimation, salivation, pupillary response, palpebral reflex, and pinna reflex. These observations were scored by type and intensity. The animals were then observed for open field behavior. Piloerection, respiratory rate, tremors, convulsions, posture, gait, ataxic gait, tail elevation, unperturbed activity level, vocalization, number of rears, fecal balls, and urine pools were all recorded during the open-field observations. Reactions to the approach of a pencil, finger snap, and tail pinch were ranked and recorded. Finally, fore- and hindlimb grip strength , rectal temperature , and body weight were measured. Automated motor activity was assessed for 30 minutes in figure-eight mazes after the completion of the FOB.

Following the last FOB and motor activity evaluation, the rats were anesthetized with heparinized sodium pentobarbital (i.p.). The thoracic cavity was opened and the animals were infused with phosphate-buffered gluteraldehyde through the left ventricle. The perfused brain, spinal cord, and sciatic nerve with its tibial, sural, and peroneal divisions were removed. The brain and nerve tissues were processed for embedding in paraffin or glycol methacrylate (dorsal root ganglia and peripheral nerves) and sectioned for light or electron microscopic pathologic evaluation.

Type: 90-Day Neurotoxicity
Species/strain: Rat/Sprague-Dawley; Tac:N(SD)fBR
No./sex/dose: 10/sex/group
Vehicle: None
Method: USEPA 1984, 40CFR Part 798:6050, 6400, and 6200

**Result** : Motor activity in a figure-eight maze and unperturbed activity in the FOB were decreased at week 4 in females exposed to 7060 ppm; activity in the FOB was also decreased in females exposed to 450 ppm at week 4. Other changes in the FOB appeared to be minor, and no changes were observed during microscopic examination of tissues from the nervous system.

**Test substance** : Diisopropyl Ether (CAS No. 108-20-3); purity ~92%.

**Conclusion** : Inhalation exposures to DIPE at concentrations as high as 7060 ppm for 13 weeks resulted in few observable effects on the nervous system.

**Reliability** : (2) valid with restrictions
GLP unknown. Study well documented, meets generally accepted scientific principles, acceptable for assessment.

01.11.2005 (26)

## 5.5 GENETIC TOXICITY 'IN VITRO'

**Type** : Bacterial reverse mutation assay

| | | |
|---|---|---|
| **System of testing** | : | Salmonella typhimurium |
| **Test concentration** | : | Up to 8000 ug/ml in the pre-incubation mix |
| **Cycotoxic concentr.** | : | |
| **Metabolic activation** | : | with and without |
| **Result** | : | negative |
| **Method** | : | other: Similar to OECD Guideline 471 |
| **Year** | : | 1988 |
| **GLP** | : | no data |
| **Test substance** | : | other TS: Diisopropyl ether (CAS No. 108-20-3) |

**Remark** : Strains tested: Salmonella typhimurium tester strains TA98, TA100, TA1535, TA1537, TA1538

Exposure method: Preincubation assay for volatile compounds [Brooks and Dean 1981]

Test Substance Doses/concentration levels: Up to 8000 ug/ml in the pre-incubation mix

Metabolic activation: With and without (S9 fraction mix of livers of Aroclor 1254 pretreated rats)

Vehicle: Tween 80/ethanol

Tester strain, activation status, Positive Controls and concentration level: Not stated

Statistical analysis: Mean revertant colony count and standard deviation were determined for each dose point.

Dose Rangefinding Study: Cytotoxicity study

S9 Optimization Study: No

| | | |
|---|---|---|
| **Result** | : | DIPE did not induce reverse gene mutation in any strain. The test substance was not genotoxic in this assay with or without metabolic activation. |
| **Test substance** | : | Diisopropyl ether (CAS No. 108-20-3)<br>Chemical Name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-<br>Source/purity not specified. |
| **Conclusion** | : | Under the conditions of this study, the test material was not mutagenic. |
| **Reliability** | : | (2) valid with restrictions<br>Restriction due to the lack of any information regarding the selection of dose levels used during the study. In addition no information is presented regarding cytotoxicity or the presence of test material precipitate in the cultures. Although study was not stated to be conducted under GLP, it was conducted at a reputable laboratory [Shell Research Limited, Sittingbourne Research Center]. |

10.11.2005 (4)

| | | |
|---|---|---|
| **Type** | : | Sister chromatid exchange assay |
| **System of testing** | : | Chinese hamster ovary cells |
| **Test concentration** | : | Up to 1200 ug/ml |
| **Cycotoxic concentr.** | : | |
| **Metabolic activation** | : | without |
| **Result** | : | negative |
| **Method** | : | other: Similar to OECD Guideline 473 |
| **Year** | : | 1984 |
| **GLP** | : | no data |
| **Test substance** | : | other TS: Di-isopropyl ether (CAS No. 108-20-3) |

**Remark** : Test type: Chromosome damage

Exposure method: For volatile compounds

Metabolic activation: Metabolic activation S9 was not added because liver cells are metabolically competent

Vehicle: Tween 80/ethanol

Tester strain, activation status, Positive Controls and concentration level: Cultured CHO cells were grown in 80 cm2 flasks for 24 hr before compound treatment. Treatment periods were 5 hr in the presence of S9 mix and 24 hr in the absence of S9. Colcemid was added to all cultures 22 hr after the initial treatment. After a further 2 hr, the cells were trypsinized, resuspended in hypotonic solution and then fixed, before spotting onto slides. Cell preparations were then stained with Giemsa. The slides were randomly coded and 100 cells from each culture were analyzed microscopically. Mitotic index estimations were also made. The positive controls were ethylmethanesulfonate [-S9] and cyclophosphamide [+S9].

Vehicle control: Yes

Dose rangefinding study: Cytotoxicity study

S9 Optimization study: No

**Result** : DIPE did not induce chromosomal damage in CHO cells. The test substance was not genotoxic in this assay.

**Test substance** : Di-isopropyl ether (CAS No. 108-20-3)
Chemical Name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Source/purity of test material: 98.5%

**Conclusion** : Under the conditions of this study, the test material was not mutagenic.

**Reliability** : (2) valid with restrictions
Restriction due to the lack of any information regarding the selection of dose levels used during the study. In addition no information is presented regarding cytotoxicity or the presence of test material precipitate in the cultures. Although study was not stated to be conducted under GLP, it was conducted at a reputable laboratory [Shell Research Limited, Sittingbourne Research Center].

10.11.2005 (3)

**Type** : DNA damage and repair assay
**System of testing** : Rat liver cells
**Test concentration** : Up to 1200 ug/ml
**Cycotoxic concentr.** :
**Metabolic activation** : without
**Result** : negative
**Method** : other: Similar to OECD Guideline 476
**Year** : 1984
**GLP** : no data
**Test substance** : other TS: Di-isopropyl ether (CAS No. 108-20-3)

**Remark** : Test type: Chromosome damage

Strains tested: RL4

Metabolic activation: Metabolic activation S9 was not added because liver cells are metabolically competent.

Vehicle: Tween 80/ethanol

Tester strain, activation status, Positive Controls and concentration level: Cultured rat liver cells were grown and treated on glass microscope slides

contained in 100 ml glass Leighton tubes. After 22 hr exposure to test compound or solvent, colcemid was added to each culture. After a further 2 hr, the slides were removed, subjected to hypotonic treatment followed by fixation and stained with Giemsa. The preparations were randomly coded and 100 cells from each culture were analyzed microscopically. The positive control was 7,12-dimethylbenzanthracenene.

Vehicle control: Yes

Dose rangefinding study: Cytotoxicity study

S9 Optimization study: None needed

**Result** : DIPE did not induce chromosomal damage in rat liver cells. The test substance was not genotoxic in this assay.

**Test substance** : Di-isopropyl ether (CAS No. 108-20-3)
Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Source/purity of test material: 98.5%

**Conclusion** : Under the conditions of this study, the test material was not mutagenic.

**Reliability** : (2) valid with restrictions
Restriction due to the lack of any information regarding the selection of dose levels used during the study. In addition no information is presented regarding cytotoxicity or the presence of test material precipitate in the cultures. Although study was not stated to be conducted under GLP, it was conducted at a reputable laboratory [Shell Research Limited, Sittingbourne Research Center].

10.11.2005 (3)

**Type** : Gene mutation in Saccharomyces cerevisiae
**System of testing** : Saccharomyces cerevisiae
**Test concentration** : Up to 8000 ug/ml in the pre-incubation mix
**Cycotoxic concentr.** :
**Metabolic activation** : with and without
**Result** : negative
**Method** : other: Similar to OECD Guideline 481
**Year** : 1984
**GLP** : no data
**Test substance** : other TS: Di-isopropyl ether (CAS No. 108-20-3)

**Remark** : Test type: Yeast mitotic gene conversion

Strains tested: JD1

Exposure method: [Brooks and Dean 1981]

Metabolic activation: With and without (S9 fraction mix of livers of Aroclor 1254 pretreated rats)

Vehicle: Tween 80/ethanol

Tester strain, activation status, Positive Controls and concentration level: Yeast cells were grown in log-phase, washed and resuspended in 2/5 strength YEPD broth at a concentration of 1 X 107 cells/ml. The suspension was divided into 1.9 ml amounts in 30 ml universal containers and 0.1 ml of test compound solution was added. For experiments with metabolic activation [+S9], 0.1 ml of DIPE was added to0 1.6 ml of yeast cell suspension, together with 0.3 ml of S9 mix. Initially a range of concentrations of DIPE was tested up to 5 mg/ml if solubility allowed. A second experiment was performed based on these results and taking into account cell viability. The cultures were incubated with shaking at 30 C for 18 hr. Aliquots were plated onto the appropriate culture media for selection of mitotic gene convertants and cells surviving the treatment. Mitotic gene

conversion may be scored by supplementing the minimal medium with histidine to score tryptophan prototrophs, and with tryptophan to score histidine prototrophs. Control plates were set up with solvent alone and with the positive control compounds 4-nitroquinoline oxide and cyclophosphamide.

Vehicle control: Yes

Dose rangefinding study: Cytotoxicity study

S9 Optimization study: No

**Result** : DIPE did not induce mitotic gene conversion I yeast. The test substance was not genotoxic in this assay with or without metabolic activation.

**Test substance** : Di-isopropyl ether (CAS No. 108-20-3)
Chemical name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-
Source/purity of test material: 98.5%

**Conclusion** : Under the conditions of this study, the test material was not genotoxic.

**Reliability** : (2) valid with restrictions
Restriction due to the lack of any information regarding the selection of dose levels used during the study. In addition no information is presented regarding cytotoxicity or the presence of test material precipitate in the cultures. Although study was not stated to be conducted under GLP, it was conducted at a reputable laboratory [Shell Research Limited, Sittingbourne Research Center].

10.11.2005 (3)

## 5.6 GENETIC TOXICITY 'IN VIVO'

## 5.7 CARCINOGENICITY

## 5.8.1 TOXICITY TO FERTILITY

## 5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

**Species** : rat
**Sex** : female
**Strain** : Sprague-Dawley
**Route of admin.** : inhalation
**Exposure period** : 6 hr/day
**Frequency of treatm.** : Gestation Days 6-15
**Duration of test** : 20 days
**Doses** : 0, 430, 3095, or 6745 ppm
**Control group** : other: yes (untreated & sham-exposed)
**other: NOEL Maternal** : = 430 ppm
**other: NOEL Pup** : = 430 - ppm
**Result** : Maternal NOEL: 430 ppm; Pup NOEL: 430 ppm
**Method** : EPA OTS 798.4350
**Year** : 1996
**GLP** : no data
**Test substance** : other TS: Diisopropyl Ether (CAS No. 108-20-3)

**Method** : Statistical method:
Statistical analyses of numerical data included ANOVA and Tukey's studentized range test for data on serum chemistry. Duncan's multiple

range test was used for hematology and body weights to assess statistically significant differences between control and exposed groups. Data on the maternal biophase, cesarean sections, and fetuses were evaluated by ANOVA followed by group comparisons using Fisher's exact or Dunnett's test.

**Remark** : Nulliparous females were housed with males in a 1:1 ratio and observed daily for evidence of breeding activity. Females positive for sperm plug and for sperm in the vaginal lavage fluid were considered to be at day 0 of gestation and were individually housed. The females were then randomly distributed to 5 groups of 22 animals each: untreated controls, sham-exposed controls, and 3 groups exposed to vapors of DIDP at 430, 3095, or 6745 ppm for 6 hr/day on gestation days (GD) 6-15.

Vapors were generated by metering DIPE on to a warmed fiberglass wick and carried to the three 1m3 exposure chambers by a stream of measured and filtered room air. Temperature and humidity in the chambers were measured every 30 minutes and air flow through each chamber was metered to provide at least 12 air changes/hour. Chamber air samples were collected with a gas-tight syringe and analyzed with a gas chromatograph with a flame ionization detector and a fused silica column. Samples were periodically obtained for analysis by gas chromatography/ mass spectroscopy.

Sham-exposed and test animals were housed in their exposure chambers throughout the exposure period; untreated controls in a separate room. Food and water were not available during the 6 -hour exposure periods but were available ad libitum at all other times. All animals were observed daily. Body weights were recorded on days 0, 6, 13, 16, and 20. Food consumption was measured on GD 6, 13, 16, and 20. Females were sacrificed on GD 20 by diethyl ether overexposure followed by exsanguination. Serum samples from the descending aorta were analyzed for glucose, urea nitrogen, total protein, albumin, globulin, A/G ratio, sorbitol dehydrogenase, lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total bilirubin, creatinine, cholesterol, triglycerides, uric acid, Cl, Ca, Na, K, and P. All organs were examined grossly. The number of corpora lutea per ovary and the gravid uterine weights were recorded. Uterine contents were examined and the numbers of implantation sites, early and late resorptions, and live and dead fetuses were recorded. The gender of each fetus was recorded. Fetuses were weighed and examined for gross anomalies. Fetuses of each litter were equally distributed between two groups; half were fixed in Bouin's solution and examined for visceral anomalies and the remaining fetuses were fixed in 95% ethanol and examined for skeletal anomalies after differential staining for cartilage and bone.

Dams exposed to 6745 ppm had a slight reduction in body weight gain and a significant decrease in food consumption. A concentration-related increase in the incidence of rudimentary 14th ribs was observed (statistically significant at 3095 and 6745 ppm) but the relevance of the finding was uncertain. There was no apparent toxicity, either maternal or fetal, at the lowest exposure concentration, 430 ppm.

Type: Developmental Toxicity
Species/strain: Sprague-Dawley; VAF/Plus Crl:CD(SD)BR
No./dose: 22/group
Vehicle: None
Method: USEPA 1984; 40CFR Part 798:4350

**Result** : Maternal NOEL: 430 ppm
Pup NOEL: 430 ppm

**Test substance** : Diisopropyl Ether (CAS No. 108-20-3); purity ~92%.

**Conclusion** : DIPE is not a teratogen.

**Reliability** : (2) valid with restrictions

GLP unknown. Study well documented, meets generally accepted scientific principles, acceptable for assessment.

01.11.2005 (5)

### 5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

### 5.9 SPECIFIC INVESTIGATIONS

### 5.10 EXPOSURE EXPERIENCE

### 5.11 ADDITIONAL REMARKS

| | | |
|---|---|---|
| **Type** | : | other: Sensory Irritation in Humans |
| **Method** | : | Non-guideline. |
| **Remark** | : | Species/strain: Humans<br>Sex: Male and female<br>Number/sex/group: Average of 12<br>Route of administration: Inhalation<br>Vehicle: None<br>Control: No<br>Year: Prior to 1946<br>GLP: No |
| **Result** | : | 300 ppm: 35% of the subjects objected to this solvent because of the unpleasant odor rather than irritation.<br>500 ppm: there was a sensory response that was acceptable to the majority of subjects. |
| **Test condition** | : | Subjects were exposed for 15 minutes and olfactory fatigue and irritation of mucous membranes were reported. "Motion pictures were shown to occupy the subject's attention and divert their thoughts from the atmospheric contamination to which they were exposed." |
| **Test substance** | : | Diisopropyl ether (CAS No. 108-20-3)<br>Chemical Name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-<br>Test material is stated to be technical grade product. |
| **Conclusion** | : | DIPE does not appear to be a sensory irritant at concentrations up to 500 ppm, but it does have an unpleasant odor at this concentration. |
| **Reliability** | : | (2) valid with restrictions<br>Not GLP but conducted at a reputable laboratory [Harvard School of Public Health, Boston]. |

01.11.2005 (27)

| | | |
|---|---|---|
| **Type** | : | other: Sensory irritation in humans |
| **Method** | : | Non-Guideline. |
| **Remark** | : | Species/strain: Young adult humans [University of California staff and medical students]<br>Sex: Not specified<br>Number/sex/group: Not specified<br>Route of administration: Inhalation<br>Vehicle: None<br>Control: No<br>Year: 1955<br>GLP: No |
| **Result** | : | Numbers of subjects with degree of effect |

| | | |
|---|---|---|
| | | Concentration 400 ppm 800 ppm<br>Number subjects: 7 7<br>Eye irritation: 7 absent 3 absent, 3 slight, 1 mod.<br>Nose irritation: 5 absent, 2 slight 2 absent, 5 slight<br>Pulmonary discomfort: 7 absent 4 absent, 3 slight<br>Olfactory cognition : 1 slight, 6 mod. 4 mod., 3 severe<br>CNS effects : 7 absent 7 absent |
| **Test condition** | : | Exposures were conducted in a whole-body chamber approximately 7700 l equipped with a fan. Exposures were made in a static atmosphere generated by vaporizing a predetermined quantity of test solvent from a hot surface. Five minutes were allowed for evaporation and equilibration, and subjects were exposed for 5 minutes, during which time they noted the degree of subjective responses at one-minute intervals. |
| **Test substance** | : | Diisopropyl ether (CAS No. 108-20-3)<br>Chemical Name: Isopropyl ether; isopropoxy propane, 2-; oxybis [propane], 2,2 '-<br>Test material is stated to be commercial grade with purity of 98% or better, provided by Shell Chemical Corporation. |
| **Conclusion** | : | 400 ppm: 5 mins of inhalation exposure caused no eye irritation, none to slight nose irritation, no pulmonary discomfort, olfactory recognition but no central nervous system effects.<br><br>800 ppm: 5 mins of inhalation exposed caused slight eye and nose irritation, none to slight pulmonary discomfort, definite olfactory recognition but no central nervous system effects. |
| **Reliability** | : | (2) valid with restrictions<br>Not GLP but conducted at a reputable laboratory [University of California School of Medicine]. |

01.11.2005 (17)

## 6.1 ANALYTICAL METHODS

## 6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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## 10.1 END POINT SUMMARY

## 10.2 HAZARD SUMMARY

## 10.3 RISK ASSESSMENT